Physical activity and breast cancer survival

Commentary

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Adeyemi A Ogunleye[1] and Michelle D Holmes[1,2]

[1]Department of Epidemiology, Harvard School of Public Health, 677 Huntington Ave, Boston, MA 02115, USA
[2]Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA

Corresponding author: Michelle D Holmes, michelle.holmes@channing.harvard.edu

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Abstract

Physical activity improves quality of life after a breast cancer diagnosis, and a beneficial effect on survival would be particularly welcome. Four observational studies have now reported decreased total mortality among physically active women with breast cancer; the two largest have also reported decreased breast cancer specific mortality. The estrogen pathway and the insulin pathway are two potential mechanisms by which physical activity could affect breast cancer survival. Randomized trials are ongoing but trials of lifestyle factors are notoriously challenging to perform. Women with breast cancer have little to lose and may possibly gain from moderate exercise.

Introduction

The benefits of physical activity in preventing chronic disease are legion: improved mental health, reduced risk of cardiovascular and metabolic disease, and reduced mortality [1]. There is also interest in the ability of physical activity to prolong life in those already diagnosed with chronic disease. A beneficial effect of physical activity on breast cancer survival would be particularly welcome. Breast cancer is the most common cancer of women in the United States and is increasing in developing countries [2,3]. Length of survival after a breast cancer diagnosis varies widely, even after accounting for stage at diagnosis and treatment, suggesting other factors may also be important. Lifestyle changes are common after a cancer diagnosis, and cancer survivors report changing to increase well-being, maintain health, and prevent recurrence [4].

Incidence

It is logical to consider physical activity's influence on breast cancer survival since there is abundant evidence of a reduced risk of developing breast cancer among physically active women. A 2008 review reported that physical activity was associated with a 25 to 30% decrease in risk across 62 studies with 83% of the positive studies reporting a dose-response [5]. A systematic review reported a 15 to 20% reduction in risk of breast cancer with higher physical activity, and a risk reduction of about 6% per hour of physical activity per week [6]. The association was stronger for post-menopausal breast cancer than pre-menopausal, and there was a dose-response relationship in half of the higher quality studies that reported a decreased risk [6]. The association of physical activity with breast cancer appears consistent across levels of dietary intake, body mass index, racial groups, tumor stage and histologic sub-types [5,6].

The stronger association of physical activity with risk of post-menopausal compared with premenopausal breast cancer hints at a biological mechanism. Physical activity suppresses estrogen levels [7] and so could have a stronger effect in post-menopausal women, in whom higher estrogen levels are more strongly associated with breast cancer incidence [8].

Recurrence/survival

Physical activity improves quality of life after a breast cancer diagnosis [9]. The evidence for an association with breast cancer survival was first examined in a prospective population-based study of 412 women that found no association [10]. However, in this study physical activity was assessed before diagnosis; it is physical activity after diagnosis that is most clinically relevant to a woman facing this illness. Since then four other cohorts have reported on breast cancer death and total mortality with physical activity measured after diagnosis.

In 2,987 Nurses' Health Study (NHS) participants with 280 breast cancer deaths and 8 years median follow-up, women who exercised the equivalent of 3 to 5 hours per week of walking had half the risk of dying of breast cancer (relative risk = 0.50, 95% confidence interval 0.38 to 0.84), with no evidence for increased benefit for greater exercise [11]. This level of

exercise is similar to US Centers for Disease Control and Prevention recommendations for 2.5 hours per week of moderate aerobic activity for all adults [12]. There was also a reduced risk of breast cancer recurrence and total mortality, and the benefit of physical activity was particularly apparent among women with hormone-responsive tumors [11]. The Collaborative Women's Longevity Study (CWLS) of 4,482 women with breast cancer followed for 6 years with 109 deaths reported a comparable decreased risk of breast cancer death and total death [13].

Two smaller sized cohorts reported a decreased risk for total but not breast cancer mortality with greater physical activity: The Life After Cancer Epidemiology (LACE) study in 1,970 women, [14] and the Health, Eating, Activity and Lifestyle (HEAL) study in 933 women [15]. In addition, the HEAL study reported a greater reduction in mortality for physical activity after diagnosis (67%) compared to physical activity measured before diagnosis (31%), and a 45% decreased risk of death for women who increased their physical activity after diagnosis [15].

Mechanisms

At least two potential pathways exist by which physical activity could affect breast cancer survival; the estrogen and insulin pathways. Obesity and weight gain are known to increase estrogen levels after menopause [16] and estrogen can promote breast cancer growth [17]. Physical activity can lower blood estrogens. A randomized control trial showed that the estrogen lowering effect of physical activity was prolonged by a corresponding reduction in body fat, suggesting that changes in body fat composition may modify the physical activity-breast cancer association [7]. However, obesity and weight gain are also associated with increased levels of circulating insulin [18]. Substantial evidence suggests that elevated insulin levels or metabolic syndrome predicts decreased survival in breast cancer [19]. One, both of these pathways, and/or others could be involved in the association of physical activity and energy balance with breast cancer survival. In addition, changes in insulin-like growth factor [20], and reduced inflammation and enhanced immune function [21] could also play a role.

Challenges

Available observational studies are limited by the lack of suitable biomarkers for long-term physical activity, inadequate power and the possibility of reverse causation in studies of survival. If physical activity's benefit is primarily by suppression of estrogen, the effect may be different in the current era of widespread use of aromatase inhibitors. At least two randomized trials of physical activity after a breast cancer diagnosis that have a survival outcome are currently enrolling participants (Lifestyle Intervention Study in Adjuvant Treatment of Early Breast Cancer (LISA), and Docetaxel Based Anthracycline Free Adjuvant Treatment Evaluation, as well as Life Style Intervention (SUCCESS-C)). However, results from these trials are not expected until 2018 and 2014, respectively. The difficulties of compliance and secular trends in randomized trials of lifestyle factors are well known.

Conclusion

Despite the challenges listed above, women with breast cancer have little to lose from moderate exercise, and there is growing evidence for benefit. Physically activity in women with breast cancer is associated with better mood, body image, and self-esteem. Physical activity can reduce women's risk of other important chronic diseases, such as heart disease and diabetes. Finally, mounting data show physical activity may help women with breast cancer avoid dying from that disease.

Competing interests

The authors declare that they have no competing interests.

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